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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte OLLE KORSGREN, WILLIAM BENNET,
BO NILSSON, and ROLF LARSSON

Appeal 2009-015372
Application 09/890,936
Technology Center 1600

Before ERIC GRIMES, MELANIE L. McCOLLUM, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL[1, 2]

This is an appeal under 35 U.S.C. § 134 involving claims to a method of transplanting insulin producing cells. The Examiner rejected the claims as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.
[2] Oral Hearing held January 13, 2011.

Statement of the Case

The Specification teaches that the invention "relates to a use of a clotting preventing agent in the production of a drug for administration in connection with transplantation of cells and tissue, such as insulin producing cells in the form of isolated islets to patients with insulin dependent diabetes mellitus, IDDM" (Spec. 3).

The Claims

Claims 4, 8, 9, 11, and 27 are on appeal.[3] Independent claim 4 is representative and reads as follows:

> 4. A method comprising transplantation of insulin producing cells in the form of individually isolated islets to a patient suffering from insulin dependent diabetes mellitus (IDDM),
>
> wherein said individually isolated islets are modified by irreversible adsorption with a clotting inhibiting agent comprising heparin or a fraction or derivative thereof onto the surfaces of the islets,
>
> wherein said individual islet cells are each separately coated with heparin or a fraction or derivative thereof by preincubation of islets in an aqueous solution containing heparin or a fraction or derivative thereof,
>
> wherein said clotting inhibiting agent acts to inhibit clotting or reduce clotting.

The issues

A. The Examiner rejected claims 4, 8, 11, and 27 under 35 U.S.C. § 102(b) as anticipated by Wagner[4] (Ans. 3-4).

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[3] Claims 14 and 26 were withdrawn from consideration and the remaining claims were cancelled. (App. Br. 3.)

[4] Wagner et al., DE 19623440 A1, published Dec. 18, 1997.

B. The Examiner rejected claims 4, 8, 11, and 27 under 35 U.S.C. § 102(b) as anticipated by Soon-Shiong[5] (Ans. 4-5).

C. The Examiner rejected claims 4, 8, and 11 under 35 U.S.C. § 102(b) as anticipated by Nomura[6] (Ans. 5-6).

D. The Examiner rejected claim 9 under 35 U.S.C. § 103(a) as obvious over Soon-Shiong, Wagner, and Couser[7] (Ans. 6-8).

A. 35 U.S.C. § 102(b) over Wagner

The Examiner finds that "Wagner et al. teach method of use of anticoagulants such as heparin, hirudin and Marcumar and derivatives thereof in connection with transplantation of insulin producing cells such as islets of Langerhans" (Ans. 4). The Examiner finds that "Wagner discloses that the islets may be microencapsulated. Additionally, if the cells are microencapsulated, they are first mixed with the anticoagulant material. This step of mixing the anticoagulant material anticipates the herein rejected claims" (Ans. 4).

Appellants contend that the "[n]owhere in Wagner is it even remotely suggested that the islets be coated in the sense of the present invention" (App. Br. 15). Appellants contend that "there is a fundamental difference between encapsulation (the closest Wagner comes to the present invention)

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[5] Soon-Shiong et al., US 5,705,270, issued Jan. 6, 1998.
[6] Nomura et al., *Unpurified Islet Cell Transplantation in Diabetic Rats*, 28 TRANSPLANTATION PROCEEDINGS 1849-1850 (1996).
[7] Couser et al., *The Effects of Soluble Recombinant Complement Receptor 1 on Complement-Mediated Experimental Glomerulonephritis*, 5 J. AM. SOC. NEPHROLOGY 1888-1894 (1995).

and modification by irreversible absorption of a clotting inhibiting agent in accordance with the present invention and as claimed" (App. Br. 20).

Appellants cite to the Korsgren Declaration,[8] which states "as fact that coating according to our invention is absolutely not the same as encapsulating according to Wagner and Soon-Shiong" (Korsgren Dec. 2). The Korsgren Declaration states that in the instant invention "the surface of each individual islet is modified to reduce thrombogenicity, and each islet is free to interact with the biological environment. No physical barrier and no immunological barrier occur in our invention" (Korsgren Dec. 6).
The Shapiro Declaration[9] states that "adsorption of clotting inhibiting agent onto the individual isolated islets is quite different from islet encapsulation, the latter of which refers specifically to immunological isolation of islets from attacking immune damaging cells" (Shapiro Dec. 3).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Wagner anticipates the method of claim 4?

Findings of Fact

1. Wagner teaches that in "micro-capsulation, individual islets are enclosed in the smallest possible capsules made of alginate complexed with polylysine and transplanted . . . The results however cannot be reproduced in a uniform manner as the capsulation technology so far has not been standardized" (Wagner 6).

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[8] The Korsgren Declaration was filed on March 2, 2004.
[9] The Shapiro Declaration was filed on Dec. 10, 2007.

2. Wagner teaches that the "invention focuses on combating the inhibitive effects of blood constituents on the surface of the membrane" (Wagner 9).

3. Wagner teaches that "[a]dsorption of proteins may be seen as the obligatory response of blood to an artificial surface . . . All this inevitably leads to the formation of thrombus as a result of which, during clinical application, a pharmacotherapy with anticoagulants, platelet aggregation inhibitors, and plasminogen activators become necessary as simultaneous treatment" (Wagner 11-12).

4. Wagner teaches that the "immobilization system contains components, which either suppress or prevent agglomeration of the blood" (Wagner 31, claim 6).

5. Wagner teaches that the "product is characterized by the fact that Heparin, Hirudin, Marcumar or their derivatives and/or modifications are used to antagonize agglomeration" (Wagner 31, claim 7).

Principles of Law

"[A]nticipation of a claim under § 102 can be found only if the prior art reference discloses every element of the claim …." *In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986) (*citing Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984)). "[A]bsence from the reference of any claimed element negates anticipation." *Kloster Speedsteel AB v. Crucible, Inc.*, 793 F.2d 1565, 1571 (Fed. Cir. 1986).

Analysis

Claim interpretation is at the heart of patent examination because before a claim is properly interpreted, its scope can not be compared to the prior art. In this case, Appellants challenge the Examiner's interpretation of the phrase "islets are modified by irreversible adsorption with . . . heparin" as recited in Claim 4, arguing that the "[n]owhere in Wagner is it even remotely suggested that the islets be coated in the sense of the present invention" (App. Br. 15).

During prosecution, claim terms are given their broadest reasonable interpretation as they would be understood by persons of ordinary skill in the art in light of the Specification. Therefore, we first turn to the Specification to determine whether the meaning of the phrase "islets are modified by irreversible adsorption with . . . heparin" can be discerned.

The Specification teaches the "islet cells are coated with heparin or fractions or derivatives thereof by preincubation of islets in a solution containing heparin or fractions or derivatives thereof." (Spec. 3). The Specification teaches that "adult porcine islets were modified by irreversible adsorption of the heparin conjugate onto the surface of the islets. This was accomplished by incubating the islets for 30 minutes at 37°C in a buffered saline solution containing heparin conjugate" (Spec. 9-10).

We therefore interpret the phrase "islets are modified by irreversible adsorption with . . . heparin" as requiring direct binding of the islets with heparin, consistent with the teachings in the Specification. This interpretation is supported by the Shapiro Declaration, which states that

"adsorption of clotting inhibiting agent onto the individual isolated islets is quite different from islet encapsulation, the latter of which refers specifically to immunological isolation of islets from attacking immune damaging cells" (Shapiro Dec. 3).

The Examiner does not identify any teaching in Wagner which suggests that the heparin itself is adsorbed to the islets, whether reversibly or irreversibly. At best, Wagner teaches the incorporation of heparin into a capsule which is used to encapsulate islets (FF 1-5). This is insufficient to teach the limitation requiring that "islets are modified by irreversible adsorption with . . . heparin" of claim 4.

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that Wagner anticipates the method of claim 4.

B. 35 U.S.C. § 102(b) over Soon-Shiong

The Examiner finds that "Soon-Shiong et al. teach microcapsules containing biological material such as islet of Langerhans cells coated with polymerizable materials (see abstract, see also claim 3). The microcapsules are covalently linked with heparin" (Ans. 4). The Examiner finds that while "Appellant asserts that the heparin is not in microcapsules, since Appellant is employing the Corline Heparin Conjugate, it appears that it is similarly coated, and as such, must form micro (or macro) capsules if Appellant has followed the technique of Corline Systems AB as recited in Appellants' specification" (Ans. 5).

Appellants contend that "Soon-Shiong relates to encapsulation of the islets, something fundamentally different from the present invention as

already explained above, and as established by the evidence of the declarations of record also referred to above" (App. Br. 32). Appellants contend that there "is no reasonable certainty that anything done by Soon-Shiong and disclosed in Soon-Shiong would provide anything identical or even similar to the present invention" (App. Br. 34). Appellants contend that "there is no disclosure and no teaching how heparin could be applied to individual islets" in Soon-Shiong (App. Br. 34).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Soon-Shiong anticipates the method of claim 4?

Findings of Fact

6. Soon-Shiong teaches that "[m]icrocapsules or macrocapsules prepared by the invention process are useful for a variety of therapeutic applications, such as the encapsulation of islets of Langerhans for the treatment of diabetes" (Soon-Shiong, col. 4, ll. 1-4).

7. Soon-Shiong teaches that the "process of synthesizing the polymerizable biocompatible material comprises chemically modifying biocompatible material . . . and then contacting the resulting modified biocompatible material with a free radical initiating system under free radical producing conditions" (Soon-Shiong, col. 6, ll. 44-50).

8. Soon-Shiong teaches that "[e]xamples of biocompatible materials include . . . heparin" (Soon-Shiong, col. 6, ll. 55-60).

9. The Examiner finds that "since Appellant is employing the Corline Heparin Conjugate, it appears that it is similarly coated, and as such, must form micro (or macro) capsules if Appellant has followed the

technique of Corline Systems AB as recited in Appellants' specification" (Ans. 5).

Analysis

As discussed above, we have already interpreted the phrase "islets are modified by irreversible adsorption with . . . heparin" as requiring direct binding of the islets with heparin, consistent with the teachings in the Specification.

Soon-Shiong teaches the formation of microcapsules or macrocapsules which may incorporate heparin (FF 6-8), but Soon-Shiong does not teach direct adsorption of the heparin to the isolated islets as required by claim 4.

The Examiner finds that "since Appellant is employing the Corline Heparin Conjugate, it appears that it is similarly coated, and as such, must form micro (or macro) capsules if Appellant has followed the technique of Corline Systems AB as recited in Appellants' specification" (Ans. 5).

We are not persuaded. The Specification teaches that "[p]orcine islets were surface modified by incubation in a buffered solution containing a high molecular weight conjugate of heparin (Corline Heparin Conjugate), as disclosed in WO 93/05793, and then rinsed by changing buffer several times" (Spec. 6). While the Specification teaches using the same type of heparin as that used by Soon-Shiong, the Specification directly binds the Corline Heparin Conjugate to the islets, while Soon-Shiong forms a cross-linkable material that forms a capsule (FF 7). This is consistent with the Shapiro Declaration, which states that "adsorption of clotting inhibiting agent onto the individual isolated islets is quite different from islet

encapsulation, the latter of which refers specifically to immunological isolation of islets from attacking immune damaging cells" (Shapiro Dec. 3).

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that Soon-Shiong anticipates the method of claim 4.

C. 35 U.S.C. § 102(b) over Nomura

The Examiner finds that "Nomura et al. teach islet transplantation for the treatment of type I diabetes after the islets cells were collected and administered with various doses of heparin" (Ans. 6).

Appellants contend that the "claims do not recite administering heparin. Instead, the heparin used in the present invention has been applied to the individual islets, and it is these surface-treated islets which are administered to the patient" (App. Br. 37). Appellants cite the Larsson Declaration[10] which states

> Newly relied upon Nomura… discloses only the use of heparin administered systemically. Systemic administration of heparin is likely to generate bleeding complications, and has nothing to do with our invention which relates to the use of surface-bound heparin which acts locally at the surface of the islets thus eliminating bleeding complications.

(Larsson Decl. 5 ¶ 14).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Nomura anticipates the method of claim 4?

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[10] The Declaration was filed on December 10, 2007 by Rolf Larsson.

Findings of Fact

10. Nomura teaches that

> Unpurified islets were transplanted into the portal vein through a 24-gauge cannula over 3 minutes. Fifteen minutes after the start of injection of the cells, portal vein pressure was measured. Recipients were divided into four groups. Unpurified islet transplantation (UIT) was performed with I00 U of heparin (group 1, n = 6), heparin and 200 U/kg of ATIII (group 2, n=6), or heparin and 10 mg/kg of FOY (group 3, n = 6). In group 4, 100 U of heparin was injected into the portal vein without transplantation as control (n = 5).

(Nomura 1849, col. 1).

Analysis

While Nomura is not entirely clear on the procedure performed, Nomura never discusses a preincubation of islets and heparin (FF 10). Instead, Nomura is reasonably interpreted as teaching either simultaneous injection of islets and heparin, or transplantation of islets, followed by injection of heparin.

The Examiner finds that it "is unclear to the Examiner how the heparin coated islets of the instant claims would not also generate bleeding complications" (Ans. 19). To the extent that there is a concern about bleeding, this has no bearing on anticipation but would be relevant to enablement, an issue not raised by the Examiner.

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that Nomura anticipates the method of claim 4.

D. 35 U.S.C. § 103(a) over Soon-Shiong, Wagner, and Couser

Having reversed the anticipation rejections over Soon-Shiong and Wagner for the absence of a teaching that "islets are modified by irreversible adsorption with . . . heparin" as required by Claim 4, we necessarily reverse the obviousness rejection as the Couser reference does not address this limitation.

SUMMARY

In summary, we reverse the rejection of claims 4, 8, 11, and 27 under 35 U.S.C. § 102(b) as anticipated by Wagner.

We reverse the rejection of claims 4, 8, 11, and 27 under 35 U.S.C. § 102(b) as anticipated by Soon-Shiong.

We reverse the rejection of claims 4, 8, and 11 under 35 U.S.C. § 102(b) as anticipated by Nomura.

We reverse the rejection of claim 9 under 35 U.S.C. § 103(a) as obvious over Soon-Shiong, Wagner, and Couser.

REVERSED

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